

## SERUM DIOXIN CONCENTRATIONS AND RISK OF DIABETES IN THE SEVESO WOMEN'S HEALTH STUDY

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**Background and Aims:** 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD), a widespread environmental contaminant, is a known endocrine disruptor. Animal evidence suggests TCDD affects glucose transport and increases lipids and blood pressure. Limited epidemiologic studies suggest an association between dioxin and diabetes, but no studies have included women.

On July 10, 1976, as a result of a chemical explosion, residents of Seveso, Italy, experienced the highest levels of TCDD in a human population. In 1996, we initiated the Seveso Women's Health Study (SWHS), a retrospective cohort study of the reproductive health of the women. In 2008, we followed up the SWHS cohort. We examined the relation of TCDD exposure with diabetes over the 32 year follow-up period.

**Methods:** In 1996, we enrolled 981 women who were 0 to 40 years in 1976, resided in the most contaminated areas, Zones A and B, and had adequate archived sera collected soon after the explosion. For each woman, TCDD concentration was measured in archived serum by high-resolution mass spectrometry. A total of 833 women (85%) participated in the 2008 follow-up study. Diabetes cases were defined by self-report of diagnosis or fasting serum glucose  $\geq 126$  mg/dL at follow-up. We examined the relation of serum TCDD with diabetes using the Cox proportional hazards regression model.

**Results:** In total, 53 (5.4%) cases of diabetes were diagnosed. The geometric mean serum TCDD level for the 53 cases ( $45.9 \pm 3.6$  ppt, lipid-adjusted) was significantly lower than for non-cases ( $n=927$ ,  $71.2 \pm 4.2$  ppt) (ANOVA for  $\log_{10}$ TCDD:  $p = 0.03$ ). The unadjusted hazard ratio for diabetes associated with a ten-fold increase in serum TCDD concentration ( $\log_{10}$ TCDD) was non-significantly decreased to 0.78 (95% CI 0.47, 1.31).

**Conclusions:** Preliminary analyses suggest an inverse association between serum TCDD and diabetes in the SWHS. Multivariate results will be presented and interpreted in light of study advantages and limitations.